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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/841,580	04/24/2001	Andrea Califano	YOR920000687US2	5406
7590 01/19/2006			EXAMINER	
Ryan, Mason & Lewis, LLP			CLOW, LORI A	
Suite 205			ART UNIT	
1300 Post Road			PAPER NUMBER	
Fairfield, CT 06430			1631	
DATE MAILED: 01/19/2006				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/841,580

Applicant(s)

CALIFANO ET AL.

Examiner

Lori A. Clow, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 21 November 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-3, 17-19, 23-25 and 29 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 17-19, 23-25 and 29 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 24 April 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Applicants' response, filed 21 November 2005, has been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 1-3, 17-19, 23-25, and 29 are currently pending. Claims 4-16, 20-22, and 26-28 have been cancelled.

### **Claim Rejections - 35 USC § 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 17-19, 23-25, and 29 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, for the reasons set forth in the Office Action of 21 December 2004 and re-iterated below. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to transform data that transforms gene expression signals. For the reasons discussed below, this constitutes undue experimentation.

b) and c) The specification at page 4, beginning line 20, states the following, for example:

**"Generally, the present invention applies a transformation to convert a probability distribution of gene expression signals in control samples to a uniform distribution. The uniform distribution allows better comparisons between expression levels for genes. The transformation is derived from gene expression signals of control data and is applied to gene expression signals of phenotype data. The phenotype data can be represented in a matrix format. A number of gene expression patterns may be determined (in the form of submatrices) that will characterize the phenotype. The uniform distribution helps in this regard as it allows better comparisons of patterns. The gene expression patterns can then be used to classify samples as belonging to the phenotype set".**

The specification does not teach how to derive a transformation that transforms gene expression signals. Instead, as recited above, the specification teaches applying a transformation to convert a probability distribution of gene expression signals in control samples to a uniform distribution. The uniform distribution is then used for the comparison of expression levels in genes to elucidate patterns to then classify samples as belonging to a phenotype set.

Further, the specification teaches the following at page 6, beginning line 21:

“Basically, the present invention is used to take an initial set of expression data for one phenotype (generally called the control set and containing information from healthy cells) and to determine transformations from this data. The transformations are applied to a set of expression data from another phenotype (generally called the phenotype set and containing information from unhealthy cells). **The transformed set of data is used to determine gene expression patterns that are characteristic of the phenotype. New expression data from samples that have an unknown genetic makeup are compared with the gene expression patterns**”.

The instant claims are not drawn to comparison of any control transformation for phenotypes or comparison with unhealthy cells to determine gene expression patterns. It is unclear in the instant **claims** how one is to use a uniform distribution of unknown gene expression signals. The instant specification sheds no light on how to perform such a method, except for when the method is directed to transformation of control samples and phenotype data, as taught in the above excerpts.

d) The claims are drawn to a method for transforming gene expression signals by somehow deriving a transformation that transforms the plurality of gene expression signals into a uniform distribution which is then used to determine gene expression signals.

e) and g) The prior art does not teach transforming gene expression signals and using a uniform distribution for the determination of gene expression signals.

f) The skill of those in the art of bioinformatics is high.

h) The claims are not commensurate in scope with the specification for the reasons stated above. The skilled practitioner would first turn to the instant specification for guidance to practice said methods. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled practitioner would turn to the prior art for such

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guidance, however, the prior art does not teach such a method. Finally, said practitioner would turn to trial and error experimentation. Such represents undue experimentation.

### **Response to Applicant's Arguments**

A. Applicant “notes that ‘a transformation is derived from gene expression signals of control data and is applied to gene expression signals of phenotype data’. Thus, a transformation is first derived utilizing control data. The transformation is then applied to phenotype data. Once the transformation is applied, better comparisons can be performed. Thus the transformation occurs *prior* to the comparison” (italics supplied by Applicant).

This is not persuasive. As outlined above, the instant **claims** are drawn to deriving a transformation for transforming the plurality of gene expression signals into transformed gene expression signals for the gene. The claims do not contain the limitation that the gene expression signals of control data are transformed and then applied to gene expression signals of phenotype data. The claims are not commensurate in scope with the specification, which clearly teaches that this invention is enabled for classifying a set of phenotype data. Whether or not the transformation occurs prior to the comparison, the claims are still not enabled because one of skill in the art would not know how to use this invention. The Examiner maintains, based upon the teachings in the specification, that in order to use the invention, a comparison of transformations from a known set be made to establish the classification of the transformed unknown signals.

B. Applicant argues that “the claims have been amended to emphasize that the transformation enables the comparison step”. This is not persuasive because the claims do not

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distinguish what is being compared. There are no limitations to control sets or phenotype sets and therefore, the claims are not enabled.

C. Applicant notes that “the transformation is a tangible and useful result and that the actual step of comparison is not necessary to produce the derived transformation”. This is not persuasive. The rejection set forth above is one of enablement under 35 USC 112, 1<sup>st</sup> paragraph and not one of Utility under 35 USC 101 (e.g. tangible and useful).

### **Claim Rejections - 35 USC § 112**

The outstanding rejection under 35 USC 112, 2<sup>nd</sup> has been withdrawn in view of the claim amendments.

No claims are allowed.

### **Inquiries**

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, Ph.D., can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of

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January 11, 2006

Lori A. Clow, Ph.D.

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*Patent Examiner*

*Lori A. Clow*